

Kenneth A. Jones, et al.
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Please insert Figures 25A-25D attached hereto as **Exhibit 2**.

In the Claims:

Please amend claims 208, 213, 224, and 231 as follows:

208. (Twice Amended) A process for determining whether a chemical compound is an agonist of a mammalian GABA_BR1/R2 receptor which comprises contacting cells containing nucleic acid encoding, and expressing on their cell surface, the GABA_BR1/R2 receptor, wherein such cells prior to being transfected with such nucleic acid do not express the GABA_BR1/R2 receptor, with the compound under conditions permitting the activation of the GABA_BR1/R2 receptor, and detecting an increase in activity of the GABA_BR1/R2 receptor, so as to thereby determine whether the compound is an agonist of a GABA_BR1/R2 receptor, wherein the mammalian GABA_BR1/R2 receptor comprises a GABA_BR1 polypeptide and a GABA_BR2 polypeptide, which GABA_BR1 polypeptide has an amino acid sequence identical to the amino acid sequence shown in Figures 24A-24D (SEQ ID NO: 48) or Figures 25A-25D (SEQ ID NO: 49), and which GABA_BR2 polypeptide has an amino acid sequence (a) identical to the amino acid sequence shown in Figures 4A-4D (SEQ ID NO: 4) or Figures 23A-23D (SEQ ID NO: 47), or (b) encoded by a nucleic acid sequence identical to the receptor-encoding nucleic acid sequence contained in plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) or in plasmid BO-55 (ATCC Accession No. 209104) [, or (c) which varies from one of the amino acid sequences of (a)

or (b) in terms of the identity or location of an amino acid residue without changing the properties of the GABA_BR2 polypeptide].

213. (Twice Amended) A process for determining whether a chemical compound activates a mammalian GABA_BR1/R2 receptor, which comprises contacting cells producing a second messenger response and expressing on their cell surface the GABA_BR1/R2 receptor, wherein such cells prior to being transfected with such nucleic acid do not express the GABA_BR1/R2 receptor, with the chemical compound under conditions suitable for activation of the GABA_BR1/R2 receptor, and measuring the second messenger response in the presence and in the absence of the chemical compound, a change in the second messenger response in the presence of the chemical compound indicating that the compound activates the GABA_BR1/R2 receptor, wherein the mammalian GABA_BR1/R2 receptor comprises a GABA_BR1 polypeptide and a GABA_BR2 polypeptide, which GABA_BR1 polypeptide has an amino acid sequence identical to the amino acid sequence shown in Figures 24A-24D (SEQ ID NO: 48) or Figures 25A-25D (SEQ ID NO: 49), and which GABA_BR2 polypeptide has an amino acid sequence (a) identical to the amino acid sequence shown in Figures 4A-4D (SEQ ID NO: 4) or Figures 23A-23D (SEQ ID NO: 47), or (b) encoded by a nucleic acid sequence identical to the receptor-encoding nucleic acid sequence contained in plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) or in plasmid BO-55 (ATCC Accession No. 209104)

[, or (c) which varies from one of the amino acid sequences of (a) or (b) in terms of the identity or location of an amino acid residue without changing the properties of the GABA_BR2 polypeptide].

224. (Twice Amended) A method of screening a plurality of chemical compounds not known to activate a mammalian GABA_BR1/R2 receptor to identify a compound which activates the GABA_BR1/R2 receptor, wherein the mammalian GABA_BR1/R2 receptor comprises a GABA_BR1 polypeptide and a GABA_BR2 polypeptide, which GABA_BR1 polypeptide has an amino acid sequence identical to the amino acid sequence shown in Figures 24A-24D (SEQ ID NO: 48) or Figures 25A-25D (SEQ ID NO: 49), and which GABA_BR2 polypeptide has an amino acid sequence (a) identical to the amino acid sequence shown in Figures 4A-4D (SEQ ID NO: 4) or Figures 23A-23D (SEQ ID NO: 47), or (b) encoded by a nucleic acid sequence identical to the receptor-encoding nucleic acid sequence contained in plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) or in plasmid BO-55 (ATCC Accession No. 209104) [, or (c) which varies from one of the amino acid sequences of (a) or (b) in terms of the identity or location of an amino acid residue without changing the properties of the GABA_BR2 polypeptide,] which comprises:

(a) contacting cells containing nucleic acid encoding, and expressing on their cell surface, the GABA_BR1/R2 receptor, wherein such cells prior to being transfected with such nucleic acid do not express

the GABA_BR1/R2 receptor, with the plurality of compounds not known to activate the GABA_BR1/R2 receptor, under conditions permitting activation of the GABA_BR1/R2 receptor;

- (b) determining whether the activity of the GABA_BR1/R2 receptor is increased in the presence of the compounds, and if it is increased;
- (c) separately determining whether the activation of the GABA_BR1/R2 receptor is increased by each compound included in the plurality of compounds, so as to thereby identify the compound or compounds present in such a plurality of compounds which activates the GABA_BR1/R2 receptor.

231. (Twice Amended) A process for determining whether a chemical compound is an agonist of a mammalian GABA_BR1/R2 receptor, which comprises preparing a membrane fraction from cells which comprise nucleic acid encoding, and expressing on their cell surface, the GABA_BR1/R2 receptor, wherein such cells prior to being transfected with such nucleic acid do not express the GABA_BR1/R2 receptor, separately contacting the membrane fraction with both the chemical compound and GTPγS, and with only GTPγS, under conditions permitting the activation of the GABA_BR1/R2 receptor, and detecting GTPγS binding to the membrane fraction, an increase in GTPγS binding in the presence of the compound indicating that the chemical compound

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activates the GABA_BR1/R2 receptor, wherein the mammalian GABA_BR1/R2 receptor comprises a GABA_BR1 polypeptide and a GABA_BR2 polypeptide, which GABA_BR1 polypeptide has an amino acid sequence identical to the amino acid sequence shown in Figures 24A-24D (SEQ ID NO: 48) or Figures 25A-25D (SEQ ID NO: 49), and which GABA_BR2 polypeptide has an amino acid sequence (a) identical to the amino acid sequence shown in Figures 4A-4D (SEQ ID NO: 4) or Figures 23A-23D (SEQ ID NO: 47), or (b) encoded by a nucleic acid sequence identical to the receptor-encoding nucleic acid sequence contained in plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) or in plasmid BO-55 (ATCC Accession No. 209104) [, or (c) which varies from one of the amino acid sequences of (a) or (b) in terms of the identity or location of an amino acid residue without changing the properties of the GABA_BR2 polypeptide].

REMARKS

Claims 208, 210, 213, 214, 221-225, 228-231, and 233-240 are pending and under examination in the subject application. By this Amendment, applicants have hereinabove amended claims 208, 213, 224, and 231. Accordingly, upon entry of this Amendment, claims 208, 210, 213, 214, 221-225, 228-231, and 233-240, as amended, will be pending and under examination.

Applicants have amended the specification to include material previously incorporated by reference. Page 1, lines 17-25, of the